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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,607	10/07/2005	Michael Sturzl	0147-0265PUS1	3489

2292 7590 03/26/2007
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EXAMINER	
DANG, IAN D	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	03/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 03/26/2007.

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Office Action Summary	Application No.	Applicant(s)	
	10/537,607	STURZL ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☒ Claim(s) *10 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/03/2005 and 05/22/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *dicitionary entry, PTO-90C, and revised notice*.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 07 October 2005 has been entered in full. Claims 1, 3-6, and 13-15 are amended.

Claims 1-15 are pending and under examination.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825). See sequence compliance letter attached to the instant Office Action.

Claim Objections

Claims 2, 10 and 11 are objected to because of the following informalities:

Claim 2 seems to be missing a phrase in line 2 after the recitation of "...with the first receptor:". (Please note that claim 2, line 2 could be amended to recite, for example, "...with the first receptor, wherein step (a') and (a'') are:"

Claim 10 should recite "the second receptor for guanylate binding protein-1 or fragments of this protein is labeled", since the subject of the sentence is singular.

Appropriate correction is required.

Claim Rejections - 35 USC § 112 (Written Description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to an in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant, wherein the method comprises the steps of (a) contacting of the sample with a first receptor which specifically binds guanylate binding protein-1 or a fragment of this protein; and (b) detecting a specific binding of the receptor with guanylate binding protein-1 or a fragment of this protein. Claim 1 is drawn to fragments, any receptor, tissue sample, and body fluid. Claim 2 is drawn to proteins. Claim 4 is drawn to a surface. Claims 7-9 are drawn to a specific binding. Claim 9 is drawn to an epitope. Claim 11 is drawn to a system-emitting signal. Claim 12 is drawn to an enzyme emitting a signal. Claim 13 is drawn to any peptide, polypeptide, antibody, low molecular substance, and fragments thereof.

Thus, the claims are genus claims. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Specifically, the specification does not clearly define fragments, a receptor, a tissue sample, a body fluid, the proteins, a surface, a specific binding, an epitope, a system emitting signal, an enzyme, and a peptide,

polypeptide, antibody, low molecular substance, and fragments thereof and all methods of using such. Thus, the scope of the claims includes numerous structural and functional variants, and the genus' are highly variant because a significant number of structural and functional differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural and functional features that could distinguish fragments, a receptor, a tissue sample, a body fluid, a surface, a specific binding, an epitope, a system emitting signal, an enzyme, and a peptide, polypeptide, antibody, low molecular substance, and fragments thereof are missing from the disclosure. No common attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, fragments, a receptor, a tissue sample, a body fluid, the proteins, a surface, a specific binding, an epitope, a system emitting signal, an enzyme, and a peptide, polypeptide, antibody, low molecular substance, and fragments thereof are insufficient to describe the genus.

The written description requirement for a claimed genus' may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus for fragments, a receptor, a tissue sample, and a body fluid, the proteins, a surface, a specific binding, an epitope, a system

emitting signal, an enzyme, and a peptide, polypeptide, antibody, low molecular substance, and fragments thereof and all methods of using such.

There is no description of the special features, which are critical to the structure and function of the genus claimed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify fragments, a receptor, a tissue sample, a body fluid, the proteins, a surface, a specific binding, an epitope, a system emitting signal, an enzyme, and a peptide, polypeptide, antibody, low molecular substance, and fragments thereof encompassed by the limitations. Thus, no identifying characteristics or properties of the instant fragments, a receptor, a tissue sample, a body fluid, the proteins, a surface, a specific binding, an epitope, a system emitting signal, an enzyme, and a peptide, polypeptide, antibody, low molecular substance, and fragments thereof are provided such that one of skill would be able to predictably identify the encompassed variant biological and chemical entities recited in the methods of the instant claims. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (1) the detection of GBP-1 protein in culture medium of IFN-γ stimulated HUVEC by ELISA and immunoprecipitation (2) the detection of circulating GBP-1 in the plasma of patients treated with IFN-α by ELISA and immunoprecipitation (3) the detection of circulating GBP-1 in the plasma of patients with systemic lupus erythematosus and arthritis by ELISA and immunoprecipitation (4) the detection of circulating GBP-1 in the liquor of patients with bacterial meningitis by ELISA and immunoprecipitation, does not reasonably

provide enablement for an in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant, wherein the method comprises the steps of (a) contacting of the sample with a first receptor which specifically binds guanylate binding protein-1 or a fragment of this protein; and (b) detecting a specific binding of the receptor with guanylate binding protein-1 or a fragment of this protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

Nature of the invention and breath of the claims

The invention is drawn to an in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant, wherein the method comprises the steps of (a) contacting of the sample with a first receptor which specifically binds guanylate binding protein-1 or a fragment of this protein; and (b) detecting a specific binding of the receptor with guanylate binding protein-1 or a fragment of this protein. The invention is broad because the recitation of claims 1-15 encompasses a large number of fragments, receptors, tissue sample, and body fluid.

Unpredictability and state of the art

The state of the art for identifying and measuring the full length of guanylate binding protein-1 in tissue sample with endothelial cells or in cells cell by immunostaining is well established but the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of any tissue sample, any body fluid sample or any sample from a cell culture supernatant is not well characterized.

Sturzl et al. (US Patent 6,894,157) teach that an antibody directed against GBP-1 or parts of it can be used for the detection/quantification of GBP-1 expression (column 3, lines 13-16). In addition, Sturzl et al. recite a method for the determination of the stage of cellular differentiation can be used to detect/quantify the GBP-1 protein or fragments using inter alia GBP-1 antibodies in a Western Blot assay, immunohistochemistry, or an ELISA (column 12, lines 17-21).

GBP-1 expression has been well studied in a few cell types in response to cytokines. For instance, Lubseder-Martellato et al. (2002, cited in the IDS mailed on 06/03/2006) teach that human GBP-1 is expressed in response to IFN-γ in many cell types including endothelial cells, fibroblasts, keratinocytes, B cells, T-cells, and peripheral blood mononuclear cells (Figure 1B, page 1752). It is noted that most cells do not express GBP-1 in the absence of the stimulation of IFN-γ. The art teaches that GBP-1 is expressed only in response to stimulation of IFN-γ. However, the art is silent regarding the expression of GBP-1 in other cell types.

Although GBP-1 is present in many cell types, most data of GBP-1 have been obtained from studying its role in endothelial cells during inflammation. The studies identify and detect the presence of GBP-1 in endothelial cells in response to cytokines, such as interferon (IFN) or tumor necrosis (TNF). For instance, Guenzi et al. (2001, cited in the IDS mailed on) teach that GBP-1 expression is detected in endothelial cells by western blot and immunocytochemistry

(Figure 1, right column, page 5569) and in tissue sample immunohistochemistry (Figure 3, page 5571) with a polyclonal rabbit anti-GBP-1 antibody. The antibody was generated by using affinity-purified His6-tagged GBP-1 or a peptide with the 21 C-terminal amino acids (page 5575, right column, paragraph titled antibody production).

Furthermore, Lubeseder-Martellato et al. (2002, cited in the IDS mailed on 06/03/2006) teach that the detection and quantification of guanylate-binding protein-1 expression in HUVEC cells by immunofluorescence (Figure 2, page 1753 and Figure 4, 1755). The antibody used in the immunodetection of GBP-1 is a rat monoclonal antibody described on page 1751 (right column, 2nd paragraph titled production of rat monoclonal antibodies).

In view of these teachings in the art and the limited guidance provided in the specification, the detection of GBP-1 protein in culture medium of IFN-γ stimulated HUVEC by ELISA and the measurements of circulating GBP-1 in the plasma of patients treated with IFN-α and full length GBP-1 concentrations by ELISA are not predictable for any in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant, wherein the method comprises the steps of (a) contacting of the sample with a first receptor which specifically binds guanylate binding protein-1 or a fragment of this protein; and (b) detecting a specific binding of the receptor with guanylate binding protein-1 or a fragment of this protein.

The amount of direction or guidance present

Applicants' disclosure is limited to the detection of GBP-1 protein in culture medium of IFN-γ stimulated HUVEC by ELISA and immunoprecipitation (Figure 4, page 12) and an example for the measurements of circulating GBP-1 in the (a) plasma of patients treated with IFN-γ (Figure 5, page 12) (b) serum of patients with systemic lupus erythematosus and arthritis (figure 9, page 14), and (c) liquor of patients with bacterial meningitis (Figure 10, page 15). However, the specification does not provide guidance or direction regarding the type of receptors needed for identification of GBP-1, the detection or quantification of fragments of GBP-1, the use of receptor other than antibodies for GBP-1, the detection of GBP-1 in other cell types besides endothelial cells, in other body fluid besides serum, the detection of GBP-1 in the absence of inflammation or stimulation with interferon, and the identification of the proteins labeled prior to contacting the first receptor.

Furthermore, Applicants provide little guidance in specification to indicate which specific fragments of GBP-1 can be detected in samples, other than the full length protein.

Working Examples

Although Applicants have provided an example the detection of GBP-1 protein in culture medium of IFN-γ stimulated HUVEC by ELISA and immunoprecipitation (Figure 4, page 12) and an example for the measurements of circulating GBP-1 in the (a) plasma of patients treated with IFN-γ (Figure 5, page 12) (b) serum of patients with systemic lupus erythematosus and arthritis (figure 9, page 14), and (c) liquor of patients with bacterial meningitis (Figure 10, page 15) , the specification does not provide any other working examples for an in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in

the culture supernatant of any tissue sample, for other body fluid sample or for the culture supernatant of other cells.

In addition, the specification also does not provide working examples for the steps (a') labeling of the proteins contained in the sample or (b') labeling of the first receptor prior to contacting the first receptor.

The quantity of experimentation needed

Without sufficient disclosure in the specification, it would require undue experimentation for one of skill in the art to be able to identify and/or quantify of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant and for steps for labeling of the proteins contained in the sample or (b') labeling of the first receptor prior contacting with the first receptor. In addition, it would require undue experimentation to practice the invention commensurate in scope with the claims because, the claims are broadly drawn to an in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant, wherein the method comprises the steps of (a) contacting of the sample with a first receptor which specifically binds guanylate binding protein-1 or a fragment of this protein; and (b) detecting a specific binding of the receptor with guanylate binding protein-1 or a fragment of this protein.

Furthermore, a large quantity of experimentation is required to generate the infinite number of GBP-1 derivatives recited in the claims, to determine which specific fragments of GBP-1 can be detected in a sample, as well as to identify the first receptors would be required to detect them.

Claim Rejections - 35 USC § 112 (Second Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(i) Claims 1-15 are indefinite because the claims do not have a step that clearly relates back to the preamble of claim 1. For example, there is no step indicating how the quantification of guanylate binding protein-1 has taken place.

(ii) Claims 1-15 are indefinite because the elements recited in the claim do not constitute proper Markush groups. The claims are indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. (See especially claims 1 and 4.) See MPEP § 2173.05(h).

(iii) Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "receptor" in claims 1-15 are used by the claim to mean " antibody", while the accepted meaning is " a structural protein molecule on the cell surface or within the cytoplasm that binds to a specific factor " as recited in the Stedman's Medical Dictionary 27th edition (see attachement). The term is indefinite because the specification does not clearly redefine the term.

(iv) Claims 2, 5-8 are indefinite because it is not clear how claim 2 can comprise step (a') or (a'') prior to contacting the first receptor.

(v) Claims 2, 5-8 are rejected as being indefinite because it is not clear which proteins are to be labeled (see claim 2, step (a')). Receptors, full length GBP-1, and fragment of GBP-1 are all proteins.

(vi) Claims 5-8 recite the limitation "the surface" and "the material of the surface" (see claims 5-6, line 2). There is insufficient antecedent basis for these limitations in the claims.

(vii) Claim 8 is rejected as being indefinite because it is not clear what detection method or methods the claim is intending to encompass. For example, line 2 recites the phrase "...comprises a gel electrophoretic cleavage, optionally, furthermore, a Western blot analysis".

(vii) Claims 11-12 are rejected as being indefinite because the metes and bounds of the claims cannot be determined. See especially claim 11, line 3. Does the second receptor comprise a system emitting a signal, wherein that signal is recognized by a third receptor? Or, is the second receptor specifically recognized by a third receptor?

(ix) Claims 9-10, and 13 recite the limitation "second receptor" (see claim 9, line 3). There is insufficient antecedent basis for this limitation in these claims.

The metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country; more than one year prior to the date of application for patent in the United States.

Claims 1, 4, and 9-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Genzi et al. (cited in the IDS mailed 06/03/2005).

The claims are drawn to an in-vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample, a body fluid sample or a sample from a cell culture supernatant, wherein the method comprises the steps (a) contacting of the sample with a first receptor which specifically binds guanylate binding protein-1 or a fragment of this protein; and (b) detecting a specific binding of the receptor with guanylate binding protein-1 or a fragment of this protein. The receptor immobilized on a surface prior to contacting with guanylate binding protein-1 or fragment of this protein or the receptor is immobilized on a surface after contacting with guanylate binding protein-1 or of fragments of this protein. The detection of a specific binding of guanylate binding protein-1 or a fragment of this protein with the first receptor in step (a), the sample is contacted with the second receptor for guanylate binding protein-1 or a fragment of this protein, which binds to an epitope of guanylate binding protein-1 or a fragment of this protein, which is accessible after the binding of the first receptor to guanylate binding protein-1 or a fragment of this protein. The second receptor for guanylate binding protein-1 or fragments of this protein is labeled. The labeling of the second receptor for guanylate binding protein-1 or a fragment of this protein comprises a system emitting a signal or which is specifically recognized by a further, third receptor comprising a system emitting a signal, which includes an enzyme emitting this signal. In the method the first and the second receptor and, optionally, also the third receptor, are selected from the group consisting of peptides, polypeptides, low-molecular substances, antibodies or fragments or derivatives thereof and aptamers. The method can be an ELISA, an EIA or a RIA and can be carried out automatically.

The method further comprises step (a') or (a") prior to contacting with the first receptor (a') labeling the proteins contained in the sample or (a") labeling the first receptor. The receptor is immobilized on a surface after contacting with guanylate binding protein-1 or of fragments of this protein. The material of the surface is selected from the group consisting of sepharose, latex, glass, polystyrene, polyvinyl, nitrocellulose and silicon and a membrane, a bead, a chip or a plate. The method further comprises the step (a"') prior to the step of detection of a specific binding (a"') precipitating the beads with the complexes which are bound thereto of the first receptor and guanylate binding protein-1 or a fragment of this protein and the detection of the specific binding in step (b) comprises a gel electrophoretic cleavage, optionally, furthermore, a Western blot analysis.

Guenzi et al. teach a method of identifying guanylate binding protein 1 in a tissue sample containing endothelial cells comprising contacting the sample with a rat anti-GBP-1 and detecting binding of the antibody with goat anti rat antibodies coupled to the fluorochrome AlexaFluor 488 (page 5576, Fluorescence staining paragraph) meeting the limitations of claim 1. The receptor is immobilized onto the tissue sample after binding to the guanylated binding protein 1 meeting the limitations of claim 4.

Furthermore, upon binding of the monoclonal rat anti-GBP-1 antibody to GBP-1, GBP-1 still has other epitopes accessible to other antibodies, meeting the limitations of claim 9 (page 5576, Immunostaining of Cells or Fluorescence Staining titled paragraph). The second receptor the GBP-1 is coupled labeled with a fluorochrome (AlexaFluor 488 and AlexaFluor 546) or with a biotinylated antibody present in the ABC Elite kits the system emitting signal (page 5576, Immunostaining of Cells and Fluorescence Staining titled paragraph) meeting the limitations of

claims 10, 11 and 12. Finally, the third receptor is antibody to CD31 or Ki67 meeting the limitations of claim 13.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Guenzi et al. (2001) as applied to claims 1, 4, and 9-13 above, and further in view of Sturlz et al. (US Patent No. 6,894,157).

Sturzl et al. (US Patent No. 6,894,157) teach use of antibodies for the detection/quantification of GBP-1 expression (column 3, lines 12-16). In addition, Sturzl et al. teach the determination of the stage of cellular differentiation can also be used to detect and/or quantify the GBP-1 protein or fragments thereof using inter alia GBP-1 antibodies in a Western Blot assay, immunohistochemistry or an ELISA (column 12, lines 17-21).

It would have been obvious prima facie obvious for one of ordinary skill in the art at the time of the invention was made to measure GBP-1 by the immunodetection method ELISA taught by Sturzl et al. for an in vitro method for the identification and/or quantification of guanylate binding protein-1 or fragments of this protein in the culture supernatant of a tissue sample. One of ordinary skill in the art at the time the invention was made would been motivated to do so because the antibody to GBP-1 can be used for the detection/quantification

of GBP-1 expression (column 3, lines 14-16). One skilled in the art would have expected success because the antibody to GBP-1 has been used for detection of GBP-1 protein expression by several immunodetection methods, such as immunohistochemistry or Western blot. Accordingly, the invention taken as a whole is prima facie obvious.

Conclusion

No claim is allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ian Dang
Patent Examiner
Art Unit 1647
March 14, 2007

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER

UNITED STATES DEPARTMENT OF COMMERCE
U.S. Patent and Trademark Office
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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/537,607	10/07/2005	STURZL et al.	0147-0265PUS1

EXAMINER	
Ian Dang	
ART UNIT	PAPER
1647	20070305

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner for Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

At page 15 of the specification, the 2 oligonucleotides used for generating the construct pro3757-GBP-1 have not been assigned any SEQ ID No. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

APPLICANT IS GIVEN ONE MONTH FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.F.R.. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER

Notice to Comply	Application No. 10/537,607	Applicant(s) STURZL ET AL.	
	Examiner Ian Dang	Art Unit 1647	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e). The correct SEQ ID NO:2 is present in the paper copy of the of the sequence listing only. Therefore a search of the correct sequence is not possible.

☒ 7. Other: The 2 oligonucleotides disclosed at page 15 of the specification have not been assigned any SEQ ID No.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
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STEDMAN'S *The Best Words in Medicine.™*

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receptor (re-sep'tor, tor)

1. A structural protein molecule on the cell surface or within the cytoplasm that binds to a specific factor, such as a drug, hormone, antigen, or neurotransmitter. **2.** C. Sherrington term for any one of the various sensory nerve endings in the skin, deep tissues, viscera, and special sense organs. [L. receiver, fr. *recipio*, 1 to receive]

adrenergic *r.* reactive components of effector tissues, most of which are innervated by adrenergic postganglionic fibers of the sympathetic nervous system. Such *r.* can be activated by norepinephrine and/or epinephrine and by various adrenergic drugs; *r.* activation results in a change in effector tissue function, such as contraction of arteriolar muscles or relaxation of bronchial muscles; adrenergic *r.* are divided into &alpha (α)-*r.* and beta-*r.*, on the basis of their response to various adrenergic activating and blocking agents. SYN: adrenoceptor, adrenoreceptors.

&alpha (α)-adrenergic *r.* adrenergic *r.* in effector tissues capable of selective activation and blockade by drugs; conceptually derived from the ability of certain agents, such as phenoxybenzamine, to block only some adrenergic *r.* and of other agents, such as methoxamine, to activate only the same adrenergic *r.*. Such *r.* are designated as &alpha (α)-receptors. Their activation results in physiologic responses such as increased peripheral vascular resistance, mydriasis, and contraction of pilomotor muscles.

beta-adrenergic *r.* adrenergic *r.* in effector tissues capable of selective activation and blockade by drugs; conceptually derived from the ability of certain agents, such as propranolol, to block only some adrenergic *r.* and of other agents, such as isoproterenol, to activate only the same adrenergic *r.*. Such *r.* are designated as beta-receptors. Their activation results in physiologic responses such as increases in cardiac rate and force of contraction ($beta_1$), and relaxation of bronchial and vascular smooth muscle ($beta_2$) contained in skeletal muscle.

AMPA *r.* a type of glutamate *r.* that participates in excitatory neurotransmission and also binds &alpha (α)-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (propionic acid) and acts as a cation channel. SYN: quisqualate *r.*.

angiotensin *r.* cell-surface G-protein–coupled *r.* that mediate the effects of angiotensin (angiotensin II). Two types are recognized: AT_1 and AT_2; the former mediates the powerful vascular smooth-muscle contraction responsible for the hypertensive response produced by angiotensin (angiotensin II); the latter is not sufficiently understood to be assigned any physiologic function.

ANP *r.* cell surface *r.* for atrial natriuretic peptide that have a single transmembrane spanning element; these have integral kinase and guanylate cyclase (guanylate cyclase) domains.

ANP clearance *r.* cell surface proteins that bind atrial natriuretic peptide and ANP fragments without initiating biologic action.

asialoglycoprotein r. a surface *r.* found in hepatocytes that binds galactose-terminal glycoproteins; thus, this *r.* removes those proteins from circulation and they are in turn acted upon by hepatocyte lysosomes.
B cell r. a complex comprising a membrane-bound immunoglobulin molecule and two associated signal-transducing &alpha (α) and beta chains.
cholinergic r. chemical sites in effector cells or at synapses through which acetylcholine exerts its action.
epidermal growth factor r. (EGFR) *r.* often upregulated in epithelial tumors.
estrogen r. *r.* for estrogens; its presence conveys a better prognosis for breast cancers.
Fas r. See Fas.
Fc r. *r.* present on a variety of cells for the Fc fragment of immunoglobulins. These *r.* recognize immunoglobulins of the IgG and IgE class.
kainate r. a type of glutamate *r.* that participates in excitatory neurotransmission and also binds kainate and acts as a cation channel; injection of kainate causes death of neurons but preserves glial cells and axons.
laminin r. a *r.* found in many cell types that binds laminin and has a role in cell attachment and neurite outgrowth.
L-AP$_4$ r. a type of glutamate receptor that also binds a particular synthetic agonist and acts as a cation channel.
low-density lipoprotein r. *r.* on the surface of cells, especially liver cells, which bind to low-density lipoprotein and promote clearance of LDL from the plasma.
mannose-6-phosphate r. (MPR) *r.* in Golgi apparatus to which newly synthesized proteins that are destined to enter lysosomes bind.
metabotropic r. a type of *r.* that is linked to intracellular production of 1,2-diacylglycerol and inositol 1,4,5-trisphosphate. [metabolism + G. trope, turning, inclination, + -ic]
muscarinic r. membrane-bound proteins whose extracellular domain contains a recognition site for acetylcholine (ACh); combination of Ach with the *r.* initiates a physiologic change (slowing of heart rate, increased glandular secretory activity, and stimulation of smooth muscle contractions); changes are observed after treatment with the mushroom alkaloid muscarine. Muscarinic *r.* are to be distinguished from nicotinic *r.*.
nicotinic r. a class of cholinergic *r.* on skeletal muscle cells that are linked to ion channels in the cell membrane.
nicotinic cholinergic r. a class of *r.* responsive to acetylcholine that also are activated by nicotine; ganglionic (including the adrenal medulla) and neuromuscular *r.*. Two classes exist: nicotinic-neuronal and nicotinic-muscular.
NMDA r. a type of glutamate *r.* that participates in excitatory neurotransmission and also binds *N*-methyl-d1-aspartate; may be particularly involved in the cell damage observed in individuals with Huntington disease.
opiate r. regions of the brain that have the capacity to bind morphine; some, along the aqueduct of Sylvius and in the center median, are in areas related to pain, but others, as in the striatum, are not related.
orphan r. a nuclear *r.* for which no ligand has yet been identified.
progesterone r. intracellular *r.* for progesterone; often over-expressed in breast cancer.
quisqualate r. SYN: AMPA *r.*.
retinoic acid (retinoic_acid) r. nuclear *r.* for retinoic acid (retinoic acid).
retinoid X r. *r.* for retinoic acids; has less affinity for retinoic acid (retinoic acid) than the retinoic acid (retinoic acid) *r.* function is not yet well understood.
ryanodine r. *r.* associated with a calcium conductance channel in the sacroplasmic or endoplasmic reticulum of cells, which when

bound to ryanodine, causes the channel to remain in a subconductive state, allowing slow continuing release of calcium ions from the sarcoplasmic reticulum into the cytoplasm. The channels are normally sensitive to calcium ions and not sensitive to inositol triphosphate.
scavenger *r.* a *r.* on macrophages that binds preferentially to oxidized LDL, causing macrophages to internalize the LDL.
sensory *r.* peripheral endings of afferent neurons.
stretch *r.* *r.* that are sensitive to elongation, especially those in Golgi tendon organs and muscle spindles, but also those found in visceral organs such as the stomach, small intestine, and urinary bladder; these *r.* have the function of detecting elongation, and this distinguishes them from baroreceptors, which actually are activated by stretching of the wall of the blood vessel (blood vessel) but whose function is to elicit central reflex mechanism reducing the arterial blood pressure.
T cell antigen *r.* *r.* present on T cells that interact with both processed antigen and major histocompatibility antigens simultaneously; these are heterodimers, each consisting of either an &alpha (α) and beta chain or a &gamma (γ) and delta chain.